



2004 Selected Air Pollution Health Studies of Note: Ozone and Particulate Matter

Periodically, the American Lung Association summarizes selected studies from current research in the published literature on outdoor air pollution. These summaries are grouped below by major topic. These summaries are in no way intended to substitute for medical information from a physician, nor are they intended to represent conclusions of the American Lung Association. Citations for all studies are provided.

AIR POLLUTION AND ASTHMA

Fine Particulate Matter Correlated with Wheezing in Infants

Physicians in **Santiago, Chile** have reported that increased daily concentrations of $PM_{2.5}$ are tied to an increased risk of wheezing bronchitis in babies.

Doctors followed a group of 500 four-month old healthy infants on a monthly basis until they reached their first birthdays. They collected data on fine particulate matter, sulfur dioxide, and nitrogen dioxide from the government air monitoring network. Mobile sources, in particular diesel engines, are the major source of fine particle air pollution in Santiago and the study was conducted in an area with high-traffic density. After adjusting for sex, socioeconomic level, family history of asthma, temperature and number of siblings, they found that **a daily increase of $10 \mu\text{g}/\text{m}^3$ $PM_{2.5}$ was related to a 5 percent increase in the risk of wheezing bronchitis the next day.** The increase in wheezing was evident up to nine days after the exposures occurred. A family history of asthma also increased the risk. No association was detected with the other pollutants.

The results of this study are consistent with studies of environmental tobacco smoke exposure and lower respiratory health in young children. Multiple episodes of wheezing in the first year of life are related to an increase of asthma in older children. The researchers concluded that *“air pollution in the form of fine particulates, mostly from vehicular exhaust, may adversely affect infants’ respiratory health with potential for chronic effects later in life.”*

Pino P, Walter T, Oyarzun M, Villegas R, Romieu I. Fine particulate matter and wheezing illnesses in the first year of life. *Epidemiology* 2004; 15:702-708.

Coarse Particles Worsen Cough and Phlegm in Kids with Asthma

Even low concentrations of PM air pollution may cause symptoms of respiratory distress in children with asthma, according to a new study in **Spokane, Washington**. A panel of 16 adults and nine children with asthma kept daily diaries of their respiratory symptoms over many months. Air pollution data on various size fractions of particulate matter were collected in a city with diverse source of PM, including motor vehicles, woodstoves, agricultural burning, resuspended road dust, and dust storms.

In children, a strong association between cough and PM_{2.5} (fine particles), PM₁, PM₁₀ and PM_{10-2.5} (coarse particles) was found. Stronger associations with cough were reported for coarse particles than for fine. Increased phlegm and runny nose were associated with PM₁₀ and PM_{10-2.5}. However, no association was found between any measure of PM and respiratory symptoms in the adults. The results suggest that children are more sensitive than adults to the effects of increased levels of PM air pollution, or that the ambient air quality monitor was more representative of children's exposures, because they spend more time outdoors than adults.

Researchers concluded: *“The association between asthma aggravation and coarse particles adds to the growing literature suggesting an association between this particle size and asthma aggravation. Such a finding is physiologically feasible since particles in this size range are known to deposit in the large bronchial airways.”* Lower respiratory symptoms were more strongly associated with increases in fine particles.

Mar TF, Larson TV, Stier RA, Claiborn C, Koenig JQ. An analysis of the association between respiratory symptoms in subjects with asthma and daily air pollution in Spokane, Washington. *Inhalation Toxicology* 2004; 16:809-815.

Air Pollution Aggravates Allergies

A recent review of the effect of air pollution on allergies concludes that *“the body of current scientific data now clearly delineates the role of pollutant-mediated adverse interactions in human allergic airway diseases. The allergist-clinical immunologist should be keenly aware that both gaseous and particulate outdoor pollutants might aggravate or enhance the underlying pathophysiology of both the upper and lower airways.”*

This review article summarizes recent advances in animal toxicology, epidemiology, human exposure, and tissue and cellular studies in identifying the effects of diesel exhaust particulate matter, sulfur dioxide, nitrogen dioxide and ozone on the aggravation of asthma and allergies. It reviews potential mechanisms and discusses interactions between allergens and pollutants.

It reports, for instance, that ozone has been associated with increased risk of asthma development among children in California playing outdoor sports and that ozone can increase airway inflammation and airway responsiveness and

potentiate the airway response to inhaled allergens. Nitrogen oxides are linked to an increase in respiratory infection and wheezing and can increase the effects of inhaled allergen responses. In high concentrations, sulfur dioxide with or without exercise, is a respiratory irritant, provoking airflow limitations. Diesel exhaust particulates increase airway inflammation and can exacerbate and initiate asthma and allergies.

“As patient advocates, physicians, both individually and as members of large health organizations, should support societal control of air pollution and rally against attempts to weaken science-based regulatory air pollution standards,” conclude the authors.

Bernstein JA, Alexis N, Barnes C, Bernstein IL, Nel A, Peden D, Diaz-Sanchez D, Tarlo SM, Williams PB. Health effects of air pollution. *J Allergy Clin Immunol* 2004; 114:1116-23.

Prenatal Exposure to Air Pollution Tied to Asthma

Early exposure to air pollutants -- prenatally, and during the infant and toddler years -- can affect the lung health of babies, according to a study of pregnant women and their offspring in **New York City**.

Researchers from Columbia University gave about 300 pregnant Dominican and African-American women living in Northern Manhattan backpack size air monitors to measure their personal exposure to polycyclic aromatic hydrocarbons (PAH) for a 2-day period during their last trimester. PAHs are important components of diesel exhaust and other combustion sources.

The women were all nonsmokers and free of chronic illnesses. After the women's babies were born, researchers surveyed the mothers about the respiratory health of their children and their exposure to secondhand smoke.

At age 2, the children with the highest levels of exposure to the air pollution and the cigarette smoke were more likely to have difficulty breathing and early symptoms of asthma such as cough and wheeze. These are the first results to implicate prenatal PAH exposure, in the setting of other environmental exposures, to asthma symptoms.

The researchers conclude that *“interventions to lower the risk of respiratory disease in young children living in the inner city may need to address the importance of multiple environmental exposures.”*

Miller RL, Garfinkel R, Horton M, Camann D, Perera FP, Whyatt RM, Kinney PL. Polycyclic aromatic hydrocarbons, environmental tobacco smoke, and respiratory symptoms in an inner-city birth cohort. *Chest* 2004; 126:1071-1078.

Wintertime Air Pollution Does Not Provoke Asthma

Researchers followed a panel of 41 predominantly African-American children with moderate to severe asthma over 3 consecutive winters. The children,

ages 6-12, were enrolled in a school operated by the National Jewish Medical and Research Center in **Denver, Colorado**. Levels of criteria air pollutants were measured daily, with concurrent monitoring of lung function, bronchodilator use by inhaler and nebulizer, symptoms, and asthma exacerbations. Fifteen of the children participated in all three years of the study.

Air pollution concentrations were below the levels of the National Ambient Air Quality Standards. After controlling for upper respiratory infections, daily variability in ambient air pollutant concentrations was not associated with significant increases in asthma severity, except for a weak association between carbon monoxide and bronchodilator use.

Researchers noted that the children in the study spent much of their time indoors to avoid the colder temperatures. A follow-up study will examine the role of summertime ozone on children with asthma.

Rabinovitch N, Zhang L, Murphy JR, Vedal S, Dutton SJ, Gelfand EW. Effects of wintertime ambient air pollutants on asthma exacerbations in urban minority children with moderate to severe disease. *J Allergy Clin Immunol* 2004; 114:1131-1137.

POPULATIONS AT RISK

Air Pollution Exacerbates Cystic Fibrosis

This is the first study to investigate the impact of air pollutants on cystic fibrosis patients.

Cystic fibrosis is an inherited fatal disease with an incidence of between 1 in 2,000 to 1 in 3,200 births in the white population. As the disease progresses, it is characterized by chronic and recurrent lung infections, inflammation, and a loss of lung function over time.

Investigators at the University of Washington followed a cohort of more than 11,000 patients older than 6 years of age enrolled in the Cystic Fibrosis Foundation National Patient Registry for which medical information was available. Exposures were assessed based on air quality monitors correlated with the patients' home zip codes.

After controlling for confounders, annual average exposure to PM₁₀, PM_{2.5} and ozone was associated with an increased risk of pulmonary exacerbations. The association was most pronounced for patients who experienced two or more exacerbations per year. PM_{2.5} was also associated with a significant loss in lung function.

Researchers speculate that the decline in lung function may be due to chronic exposure to air pollutants, which may be part of the causal pathway in the worsening prognosis of cystic fibrosis.

Researchers concluded: “*Exposure to ambient PM₁₀, PM_{2.5} and ozone may increase the risk for pulmonary exacerbations and increase the rate of change in lung function in the CF (cystic fibrosis) population. Ambient air pollution may also impact survival.*”

Goss CH, Newsom SA, Schildcrout JS, Sheppard L, and Kaufman JD. Effect of Ambient Air Pollution on Pulmonary Exacerbations and Lung Function in Cystic Fibrosis. *Am J Respir Crit Care Med* 2004;169:816-821.

Deposition of Ultrafine Particles Increases in Lungs of People with Asthma

The dose of particles that reaches the lungs determines the pulmonary response to inhalation.

A group of researchers at the University of Rochester is studying the effect of ultrafine particles, those with a diameter less than 100 nanometers, on human health.

They hypothesize that ultrafine particles may contribute to the health effects of particulate matter because of their high surface area, oxidant capacity, ability to evade the macrophage defense system, and propensity for inducing pulmonary inflammation.

Earlier studies have shown that patients with chronic obstructive pulmonary disease have enhanced deposition of fine and ultrafine particles, and that fine particle deposition is increased in people with asthma. This is the first study to investigate the deposition of ultrafine particles in the lungs of subjects with mild asthma.

The study found that deposition of ultrafine particles at rest and during exercise was greater in people with asthma than in healthy subjects.

Researchers conclude: “*People with asthma have a higher respiratory dose of UFP [ultrafine particles] for a given exposure, which may contribute to their increased susceptibility to the health effects of air pollution.*”

Chalupa DC, Morrow PE, Oberdörster G, Utell MJ, Frampton MW. Ultrafine Particle Deposition in Subjects with Asthma. *Env Health Persp* 2004;112:879-882.

Overweight Children Get Higher Doses of Deposited Particles

A panel study of 36 healthy children ages 6-13 has found that obese children receive higher doses of fine particles than thin children, due to the greater volume of air they inhale and exhale. The study found that for any given height and age, the amount of air breathed in increased with increasing body mass, resulting in increased deposition of particles in the lower respiratory tract.

The rate of deposition of particles at rest was nearly three times greater in the overweight children, compared to the leanest children.

“These results suggest that overweight children may be at increased risk associated with inhaled particulate matter,” conclude the researchers.

Bennett WD, Zeman KL. Effect of body size on breathing pattern and fine-particle deposition in children. *J Appl Physiol* 2004; 97:821-826.

OZONE EXPOSURE AND MORTALITY

Ozone Linked to Higher Death Rates in Large U.S. Multi-City Study

Short-term increases in ozone were found to increase total non-accidental mortality and deaths from cardiovascular and respiratory causes in a large 14-year study of residents of **95 U.S. cities**. The relationship between mortality and ozone was evident even on days when pollution levels were below the current regulatory standard of 80 ppb averaged over 8 hours.

Researchers from Yale and Johns Hopkins University used analytical methods and databases developed for the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) to conduct their investigation.

On average across the 95 urban communities, researchers found a 0.5% increase in daily mortality when there was a 10-ppb increase in the previous week’s ozone concentration. The results indicate a substantial public health burden from ozone air pollution. **Study authors estimated that a 10 ppb increase in daily ozone would correspond to an additional 3,767 annual premature deaths in the 95 cities, but this is probably an underestimate because it only considers short-term effects.**

The ozone concentrations were not correlated with PM₁₀ in the communities studied. The analysis provided strong evidence against confounding of the effects of these two pollutants. Further, the ozone and mortality results did not appear to be confounded by temperature.

The researchers conclude: *“Our findings, interpreted in the context of the already extensive epidemiologic and toxicologic evidence on ozone toxicity, indicate that this widespread pollutant adversely affects mortality, in addition to other health effects that have been associated with ozone.”*

Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. Ozone and short-term mortality in 95 US urban communities, 1987-2000. *JAMA* 2004; 292:2372-2378.

Ozone Associated with Daily Mortality in Large European Study

A study in 23 European cities has reported a positive association between short term concentrations of ozone air pollution and daily mortality.

The Air Pollution and Health: a European Approach (APHEA2) examined data on daily ozone concentrations, daily number of deaths, confounders, and potential effect modifiers for a 3-year period in the 1990s.

During the warm season, increases in the 1-hour ozone concentrations were associated with increases in total daily deaths, in cardiovascular deaths, and in the number of respiratory deaths. Similar associations were observed with 8-hour ozone concentrations. However, no significant associations were reported for the winter months.

The associations with total mortality were independent of sulfur dioxide and PM₁₀, but were somewhat confounded by nitrogen dioxide and carbon monoxide. The dose-response relationship was linear, with the greatest effect seen on respiratory mortality.

Researchers speculate that the findings of ozone effects during the summer months may be due to higher concentrations levels, but may also be a result of higher exposures stemming from more time spent outdoors exercising. On average, effects were larger in Southern European cities, where the ozone concentrations are higher.

Gryparis A, Forsberg B, Katsouyanni K, Analitis A, Touloumi G, Schwartz J, Samoli E, Medina S, Anderson HR, Niciu EM, Wichmann E, Kriz B, Kosnik M, Skorkovsky J, Vonk JM, Dortbudak Z. Acute effects of ozone on mortality from the "Air Pollution and Health: A European Approach" project. *Am J Respir Crit Care Med* 2004;170:1080-1087.

Association Between Ozone and Mortality Not Confounded by Temperature

Large multi-center studies in the U.S. and Europe have recently reported that ozone is associated with daily deaths, especially in the summer. Since ozone air pollution peaks in the summer months, it is difficult to control for the effects of high temperature.

This study employed a "case-crossover" technique to compare each subject's characteristics and exposures at the time a death occurred, with a control period for the same subjects when the adverse event did not occur. This approach makes it possible to control for the effect of temperature on the day of death. Multiple cities must be included to provide sufficient statistical power for the analysis.

Cities studied were **Birmingham AL, Boulder CO, Canton OH, Chicago IL, Cincinnati OH, Colorado Springs CO, Columbus OH, Detroit MI, Houston TX, New Haven CT, Pittsburgh PA, Provo UT, Seattle WA, and Spokane WA.**

Close to 850,000 adult deaths were analyzed, along with data on ozone concentrations and temperature, for a 13 year period.

The author concludes that *“the association between ozone and mortality risk is unlikely to be due to confounding by temperature.”*

Schwartz J. How sensitive is the association between ozone and daily deaths to control for temperature? *Am J Resp Crit Care Med* 2004; 170: 1080-1087.

CARDIOVASCULAR EFFECTS

American Heart Association Issues Scientific Statement on Air Pollution, June 1, 2004

Exposure to air pollution contributes to the development of cardiovascular diseases, according to a new American Heart Association scientific statement published in the journal *Circulation*. The statement calls for EPA to expedite the attainment of existing National Ambient Air Quality Standards, and to strengthen the air quality standards for PM_{2.5}.

A panel of experts conducted a comprehensive review of almost 200 scientific studies on air pollution and cardiovascular disease -- including heart attacks, abnormal heart rhythms, strokes, hardening of the arteries. The statement, which was approved by the American Heart Association Science Advisory and Coordinating Committee, focuses on the dangers of particulate matter air pollution and reaffirms the dangers of environmental tobacco smoke.

The expert panel concludes that *“...the existing body of evidence is adequately consistent, coherent, and plausible enough to draw several conclusions. At the very least, short-term exposure to elevated PM significantly contributes to increased acute cardiovascular mortality, particularly in certain-at-risk subsets of the population. Hospital admissions for several cardiovascular and pulmonary diseases acutely increase in response to higher ambient PM concentrations. The evidence further implicates prolonged exposure to elevated levels of PM in reducing overall life expectancy on the order of a few years.”*

The panel calls on EPA to improve public health and substantially reduce cardiovascular deaths and disease by issuing regulations to expeditiously attain the current standards.

Furthermore the statement concludes, *“because a number of studies have demonstrated associations between particulate air pollution and adverse cardiovascular effects even when levels of ambient PM_{2.5} were within current standards, even more stringent standards for PM_{2.5} should be strongly considered by the EPA.”*

In addition, the scientists identified a number of areas for further research.

Brook RD, Franklin B, Casio W, Hong Y, Howard G, Lipsett M, Luepker R, Mittleman M, Samet J, Smith SC Tager I. Air Pollution and Cardiovascular Disease: A Statement for Healthcare Professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation* 2004;109:2655-2671.

Long-Term Exposure to Air Pollution Contributes to Very Early Stages of Artery Disease

The greater the fine particle air pollution around a person's home, the thicker the walls of their carotid arteries, the large blood vessels in the neck that carry blood to the brain, according to a University of Southern California study.

Researchers reviewed data from two clinical trials of 800 healthy people with elevated cholesterol, ages 40 and older, who lived in the **Los Angeles, California** area. The clinical trials used ultrasound to collect baseline measurements of the thickness of the inner lining of participants' carotid arteries. This provides a measure of the level of atherosclerosis in the early stages, before symptoms are evident. Atherosclerosis, or hardening of the arteries, decreases the flow of oxygen-rich blood, increasing the risk for heart pain, heart attacks, and stroke.

Researchers used ambient monitors to assign an annual mean PM_{2.5} level to the subjects' home zip codes. **After adjusting for age, smoking, and physiological factors, they found that increased artery thickness was associated with higher fine particle exposures.** The association was strongest in women over 60. *"These results represent the first evidence of an association between atherosclerosis and ambient air pollution,"* concluded the researchers. *"The findings indicate a biologically plausible link between the observed acute effects of ambient air pollution on systemic inflammation and the long-term consequences of sustained vascular inflammation leading to increased atherosclerosis and, ultimately, cardiovascular death."*

Künzli N, Jerrett M, Mack WJ, Beckerman B, LaBree L, Gilliland F, Thomas D, Peters J, Hodis HN. Ambient air pollution and atherosclerosis in Los Angeles. *Env Health Persp* 2005; 113:201-206.

Particle Pollution's Impact on Heart Comparable to Risk for Former Smokers

In a follow-up analysis to the American Cancer Society cohort study, researchers have reported a striking link between chronic exposure to fine particle air pollution and increased risk of death from cardiovascular disease in the United States.

The increased risk was comparable to that associated with being a former smoker. The new analysis is based on data collected by the American Cancer Society on the cause of death of 500,000 adults over a 16-year period, and on data on air pollution levels in cities nationwide. Data on other risk factors such as body mass, smoking, occupational exposures, and diet were also considered.

The study identifies a strong link between particulate air pollution and

ischemic heart disease (which causes heart attacks), and also a link between pollution and irregular heart rhythms, heart failure, and cardiac arrest. It also suggests general biological pathways through which pollution might cause these diseases that lead to death -- increased inflammation and nervous system aberrations that change heart rhythm. Mortality attributable to respiratory disease had relatively weak associations in this study.

Researchers conclude that “the results of this analysis are largely consistent with the proposition that the general pathophysiological pathways that link long-term PM exposure and cardiopulmonary mortality risk include pulmonary and systemic inflammation, accelerated atherosclerosis, and altered cardiac autonomic function.”

Pope CA III, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D, Godleski JJ. Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution: Epidemiological Evidence of General Pathophysiological Pathways of Disease. *Circulation* 2004;109:71-77

Blood Pressure Rises When Heart Patients Breathe Particle Pollution

Particle pollution may contribute to increased risk of cardiac illness and death in people with pre-existing heart disease, through short-term increases in systemic arterial vascular narrowing, as manifested by increased peripheral blood pressure, according to the findings of a study by Harvard University scientists.

Researchers examined blood pressure, a cardiac risk factor, and exercise data from the records of 62 **Boston** area patients who visited a hospital cardiac rehabilitation program over a three year period. Most of the patients had coronary artery disease. Data on PM_{2.5} concentrations during the five days prior to each visit were correlated with changes in blood pressure.

The study found that that increases in particulate pollution may lead to increased blood pressure when resting, and, in patients with elevated heart rate, to increased blood pressure during exercise.

Blood pressure control is an important factor in reducing cardiac morbidity and mortality following heart attacks. The study authors suggest that the changes in blood pressure might be manifestations of more widespread narrowing of the blood vessels, which could explain the reported association of pollution with increased risk of acute cardiac events in patients with preexisting heart disease.

Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, Gates KA, Hartley LH, Suh H, Gold DR. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation* 2004;110:2184-2189.

Spending Time in Traffic Triples Risk of Heart Attack

Transient exposure to traffic may trigger heart attacks in susceptible people.

The risk of a heart attack triples within an hour of being exposed to traffic pollution, whether traveling in cars, on mass transit, or by bicycle, according to a study by German researchers.

The researchers interviewed close to 700 heart attack survivors around Augsburg, Germany regarding their activities in the four days preceding the attack. The design of the study allowed for the control of other risk factors such as exercise, anger, and drug use.

A large percent of the heart attacks occurred within an hour of being in traffic. The fact that similar risks were observed for transit riders as for drivers minimizes the likelihood that the effect is entirely attributable to the stress of driving.

Researchers conclude that *“patients who are at risk for acute coronary events are likely to profit from recent efforts to improve the air quality in urban areas with the use of cleaner vehicles and improved city planning.”*

In an accompanying editorial, cardiologist Dr. Peter H. Stone of Harvard Medical School writes: *“Decades of epidemiologic evidence underscore the cardiovascular morbidity and mortality related to air pollution. The proinflammatory, proatherosclerotic, and prothrombotic effects of particulate air pollution are compelling. As both epidemiologic and now mechanistic evidence mounts, there is greater urgency to accelerate our efforts to reduce particulate air pollution and to improve cardiovascular health.”*

Peters A, von Klot S, Heier M, Trentinaglia I, Hörmann A, Wichmann HE, Löwel H. Exposure to Traffic and the Onset of Myocardial Infarction. *N Engl J Med* 2004;351:1721-30.

Stone PH. Triggering Myocardial Infarction. *N Engl J Med* 2004;351:1716-1718.

AIR POLLUTION, INFANT MORTALITY, AND CHILDREN’S HEALTH

Pediatricians Strengthen Stand on Air Pollution, December 2004

The American Academy of Pediatrics (AAP) has published an important new policy statement that strengthens its stand on the dangers that air pollution poses to children, and offers new recommendations on how to help solve the problem.

The Policy Statement, published in the December 2004 issue of *Pediatrics*, finds that there are adverse health effects at levels near or below the current standards for ozone, particulate matter, and nitrogen dioxide, and concludes that the 1997 NAAQS may not adequately protect children. It updates an earlier Policy Statement issued in 1993.

Specifically, the new Policy Statement finds that the current annual and 24-hour NAAQS for PM2.5 and PM10 should be lowered to protect public

health, based on recent scientific studies.

In addition, the policy statement cites several studies demonstrating that ozone may be toxic at concentrations lower than the current 8-hour NAAQS, and suggests that the ozone standards may need to be revised if these studies are confirmed.

The Statement makes further specific recommendations on need to set air quality standards with a margin of safety to protect against the potential effects of air pollution on the fetus, infant, and child.

Additional recommendations address the need for specific control strategies to reduce children's exposure to criteria air pollutants and toxic air pollutants, specifically mercury and diesel.

In an accompanying article, Dr. Michael W. Shannon, the chair of the AAP Committee on Environmental Health states: "*The revised standards [1997 NAAQS for ozone and PM] will protect children better than the previous standards but they still won't be adequate.*"

Committee on Environmental Health, American Academy of Pediatrics. Ambient Air Pollution: Health Hazards to Children. *Pediatrics* 2004;114:1699-1707.

Children's Immature Lungs and Undeveloped Immune Systems Render Them Vulnerable to Air Pollution

This review article by Harvard Professor Joel Schwartz distills the recent literature on the major effects of air pollution on children's health, including prenatal effects, infant mortality, acute effects, and effects of chronic exposures.

The article points out that the lung is not well formed at birth, and that the bronchial tree is still developing. **The number of alveoli in the human lung increases from 24 million at birth to 257 million at age 4.** Further, the lung epithelium is not fully developed, resulting in greater permeability in young children. Children have an immature immune system, rendering them more vulnerable to infection. Further, children spend a lot of time outdoors and breathe heavier when exercising, increasing their exposure to air pollutants.

Recent studies have reported that maternal exposure to air pollution during pregnancy is associated with adverse birth outcomes including miscarriages, premature births, and lower birth weight.

A series of innovative summer camp studies where children with asthma were subjected to air pollution all day long found that lung function declined during air pollution episodes. Other studies of asthmatic children have found that increases in several air pollutants is associated with increased levels of exhaled nitric oxide, a good marker of lung inflammation in individuals with asthma.

Longer term exposures to ozone and PM₁₀ air pollution have been correlated with lower levels of lung function growth in children, and chronic bronchitis. Rates of bronchitis and chronic cough have declined in areas where particle concentrations have fallen.

The author concludes “...*there is increasingly strong evidence that air pollution is associated with nontrivial increases in the risk of death and chronic disease in children, worse pregnancy outcomes, and exacerbation of illnesses. It is less clear which pollutants are most responsible, but particles and ozone have the strongest associations. For the incidence of asthma, traffic pollution, particularly from trucks, seems to be the key player.*”

Schwartz, J. Air Pollution and Children’s Health. *Pediatrics* 2004;113:1037-1043.

Sulfur Dioxide and Nitrogen Dioxide Identified as Risk Factors for SIDS

Ambient sulfur dioxide and nitrogen dioxide may be important risk factors for Sudden Infant Death Syndrome (SIDS) according to a time-series analysis of the twelve largest Canadian cities.

SIDS is the most common cause of death in infancy. The study design avoids confounding by differences among populations or geographic areas.

Canadian researchers collect data on daily mortality and daily air pollution concentrations during a sixteen year period. **Increased daily rates of SIDS were associated with increases, on the previous day, in the levels of sulfur dioxide, nitrogen dioxide, and carbon monoxide, but not ozone or fine particles measured every sixth day.** After adjusting for season and weather factors, the effects of NO₂ and SO₂ persisted. Researchers note that the lack of daily data for particles diminishes the power to detect an effect.

The cities studied were **Halifax, Saint John, Quebec, Montreal, Ottawa, Toronto, Hamilton, Windsor, Winnipeg, Edmonton, Calgary, and Vancouver.**

Researchers speculate that “*gaseous air pollutants may predispose subjects to episodes of apnea and/or increase the work of breathing, which may be particularly dangerous for infants with disordered ventilatory control, who may be unable to generate a sufficient compensatory response.*”

Dales R, Burnett RT, Smith-Doiron M, Stieb DM, Brooks JR. Air pollution and sudden infant death syndrome. *Pediatrics* 2004;113:628-631.

Maternal Exposure to Fine Particles Affects Developing Fetus

Personal monitors were used to assess the exposure of hundreds nonsmoking, healthy, pregnant women in **Krakow, Poland** to fine particles

over a two day period.

Total personal PM_{2.5} exposure averaged 43.1 µg/m³, with a range of 10.3-147.3 µg/m³.

After adjusting for potential confounding factors such as the size of the mother, sex of the child, gestational age, season of birth, and environmental tobacco smoke, exposure to PM_{2.5} during the second trimester of pregnancy was found to significantly lower birthweight and length at birth, as well as head circumference of newborns.

“The study provides new and convincing epidemiologic evidence that high personal exposure to fine particles is associated with adverse effects on the developing fetus. These results indicate the need to reduce ambient fine particulate concentrations,” conclude the authors.

Jedrychowski W, Bendkowska I, Flak E, Penar A, Jacek R, Kaim I, Spengler JD, Camann D, and Perera FP. Estimated risk for altered fetal growth resulting from exposure to fine particles during pregnancy: An epidemiologic prospective cohort study in Poland. *Env Health Persp* 2004; 112:1398-1402.

Expert Consensus that Particulate Air Pollution Causes Infant Mortality

The accumulated evidence indicates that children’s health is adversely affected by air pollution at levels currently experienced in Europe, according to a review by experts convened by the World Health Organization (WHO).

The experts prepared a consensus assessment of the strength of the evidence linking air pollution to various health outcomes in children.

The experts found evidence sufficient to infer a causal relationship between exposure to ambient air pollutants and:

- adverse effects on lung function development;**
- increased incidence of upper and lower respiratory symptoms;**
- aggravation of asthma (due mainly to particulate matter and ozone);**
- increased prevalence and incidence of cough and bronchitis (due to particulate matter); and**
- increased risk of respiratory death in infants.**

The experts found little evidence for a causal association between air pollution and asthma prevalence/incidence in general, except for the prevalence of asthma symptoms related to living in close proximity to traffic, which was rated as suggestive of a causal association.

Evidence was insufficient to infer a causal link between childhood cancer and outdoor air pollution at levels typically found in Europe.

The experts concluded that the evidence is sufficient to infer a causal relationship between particulate air pollution and respiratory death in infants, while for the association of birth weight with air pollution, the evidence is suggestive of causality. There was insufficient evidence to infer a causal relationship for pre-term births, intrauterine growth retardation, or birth defects.

“While recognizing the need for further research, current knowledge about the health effects of air pollution is sufficient for a strong recommendation to reduce children’s current exposure to air pollutants, in particular to the pollutants related to traffic. The experts who conducted this review consider that such reductions in levels of air pollution will lead to considerable children’s health benefit,” states the article.

Binková B, Bobak M., Chatterjee A, Chauhan AJ, Dejmek J, Dockery DW, Everard M, Forastiere F, Gilliland F, Holgate S, Johnston S, Krzyzanowski M, Kuna-Dibbert B, Maynard R, Raaschou-Nielsen O, Samet J, Schneider J, Skerrett PJ, Šrám RJ, Walters D, Weiland SK, Winneke G. WHO Monograph: The effects of air pollution on children’s health and development: a review of the evidence. WHO Regional Office for Europe 2004.

Particulate Air Pollution Is A Significant Contributor to Infant Deaths in U.S.

Twenty-four percent of infant deaths from respiratory disease, and 16 percent of sudden infant death syndrome (SIDS) fatalities may be attributable to PM₁₀, according to a study published in the online journal *Environmental Health*.

The study used exposure-response functions from an earlier U.S. cohort study to estimate the risk of infant mortality attributable to PM₁₀ in 23 U.S. metropolitan areas. The estimated number of air pollution related infant deaths was about 200 cases per year, in the 23 counties analyzed.

The following counties were included in the analysis: **Jackson, AL; Fresno, Los Angeles, Sacramento, San Diego, and San Francisco, CA; Denver, CO; Hartford, CT; Cook, Illinois; Baltimore, MD; Wayne, MI; St. Louis, MO; Bronx, Kings, and New York, NY; Philadelphia, PA; El Paso, Harris, and Dallas, TX; Oklahoma and Tulsa, OK; Providence, RI; Salt Lake City, UT; King, WA; and Milwaukee, WI.**

Approximately 75 percent of the cases were from areas where current pollution levels are estimated to be below the annual average National Ambient Air Quality Standard for PM_{2.5}. According to the authors, this suggests that *“even if all counties would comply to the new PM_{2.5} standard, the majority of the estimated burden would remain.”*

“Evidence for a causal effect of air pollution on morbidity and mortality is strong for adults, and evidence is building that air pollution has an effect on infants and young children and a potential impact during the fetal period,” the authors add.

Kaiser R, Romieu I, Medina S, Schwartz J, Krzyzanowski M, Kunzli N. Air Pollution Attributable Postneonatal Infant Mortality in U.S. Metropolitan Areas: A Risk Assessment Study. *Environmental Health* 2004;3.

Air Pollution Blamed for 6.4 Percent of Deaths in Young European Children

The World Health Organization (WHO) regional office for Europe sponsored a study of the contribution of selected environmental factors to the burden of disease among children and adolescents in Europe. Scientists used risk factors from published studies to estimate disease attributable to indoor and outdoor air pollution, inadequate water and sanitation, lead exposure, and injuries.

The study estimated that mortality attributable to short-term exposure to particulate air pollution was responsible for almost 14,000 deaths each year in Europe among children aged 0-4, though there is substantial uncertainty around this estimate. This represents a large proportion of deaths for this age group -- 6.4 percent of all deaths, or 1.8 percent of deaths due specifically to acute respiratory tract infections.

“...our findings indicate the urgent need for interventions aimed at reducing children’s exposure to unsafe water, outdoor and indoor air pollution, and lead, and at preventing injuries,” the authors concluded.

Valent F, Little D’A, Bertollini R, Nemer LE, Barbone F, Tamburlini G. Burden of disease attributable to selected environmental factors and injury among children and adolescents in Europe. *Lancet* 2004;363:2032-39.

Dirty Air Stunts Lung Growth in Teenagers

The lungs of many children who grow up in polluted areas are underdeveloped and will likely never recover, according to the latest findings of the Children’s Health Study, the longest investigation ever conducted into air pollution and kids’ health.

The study found that teenagers in smoggy communities were nearly five times as likely to have clinically low lung function, compared to teens living in low-pollution communities. Lung function in the affected children was 80 percent of the capacity expected for their age. This level of damage is similar to what is found in children whose parents regularly smoked around them.

Researchers recruited 1,759 fourth grade children from schools in 12

southern California communities and measured their lung function annually for eight years. The communities included some of the most polluted areas in the greater Los Angeles basin, as well as several low-pollution sites outside the area. Over the eight year period, researchers found that children living in the most polluted communities had significant reductions in their “forced expiratory volume” -- the volume of air that can be exhaled after taking a deep breath -- as compared to children living in cleaner communities.

In healthy people, lungs grow to full capacity during the teenage years, but typically stop growing at age 18. “*Lung development in teenagers determines their breathing capacity and health for the rest of their lives,*” said study leader John Peters, M.D., of the Keck School of Medicine at the University of Southern California.

Underpowered lungs have been shown to be second only to smoking as a risk factor for all-cause mortality, according to study author W. James Gauderman. Deficits in lung function during young adulthood can worsen respiratory conditions -- for example provoking wheezing during viral infections.

In this study, nitrogen dioxide, acid vapor, PM_{2.5}, and elemental carbon -- all products of fuel combustion -- were associated with deficits in lung function.

“Given the magnitude of the observed effects and the importance of lung function as a determinant of morbidity and mortality during adulthood, continued emphasis on the identification of strategies for reducing levels of urban air pollutants is warranted,” conclude the authors.

In an accompanying editorial, air pollution researcher C. Arden Pope III points out that there appears to be broad susceptibility to the cumulative effects of long-term repeated exposure to air pollution. “*The Children’s Health Study reports pollution-related deficits in the development of lung function in boys and girls, children with asthma and those without asthma, and smokers and nonsmokers,*” Pope states.

Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med* 2004;351:1057-67.

Pope, CA III. Air pollution and health -- Good news and bad. *N Engl J Med* 2004;351;1132-1134.

National Health Impacts for Children of Reduction in Criteria Air Pollutants

Researchers conducted a meta-analysis of studies of the impacts of ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, and fine and coarse particulate matter on children in the United States. The study was intended to estimate the benefits from reductions in criteria air pollutants due to the Clean Air Act from 1990 through 2010.

They used a methodology evolved from that used to prepare the U.S. EPA's prospective analysis of air pollution health benefits.

The study estimated that changes in criteria air pollutant concentrations would lead to 10,000 avoided asthma hospitalizations, and 40,000 fewer emergency department visits in children ages 1-16. Approximately 20 million fewer school absences can be expected, as well as 10,000 fewer low birth weight infants, and 200 fewer infant deaths.

The authors suggest that inclusion of child-specific data would add \$1-2 billion to the \$8 billion estimate in health benefits attributed to compliance with the Clean Air Act from 1990 - 2010.

Authors state that these estimates are very conservative, because they exclude certain health effects, and consider other health benefits only in specific age groups. Further, monetary estimates do not include the costs of pain and suffering, or lost leisure time. They consider their analysis to represent a starting point and as identifying key research needs in benefits evaluation.

Wong, EY, Gohlke, J, Griffith, WC, Farrow, S, and Faustman, EM. Assessing the Health Benefits of Air Pollution Reduction for Children. *Env Health Persp* 2004;112:226-232.

PARTICLE POLLUTION AND MORTALITY

Study Isolates Particle-Death Link

A study of over one million deaths in 14 U.S. cities has built the strongest case yet to pinpoint PM₁₀ as the pollutant elevating the risk of premature death, and has demonstrated that the association is not due to failure to consider the effects of other air pollutants.

Joel Schwartz, of the Harvard School of Public Health, obtained death certificate data from 14 cities where daily PM₁₀ monitoring was available (**Birmingham, AL, Boulder and Colorado Springs, CO, Canton, Columbus, and Cincinnati, OH, Chicago, IL, Detroit, MI, Minneapolis/St. Paul, MN, New Haven, CT, Pittsburgh, PA, Provo-Orem, UT, and Seattle and Spokane, WA**).

Researchers compared the air pollution on the day each person died, to the air pollution on a nearby day (in the same month of the same year) when they did not die, to see if air pollution was associated with increased death risk. Since most things that increase a person's risk of dying (smoking history, obesity, etc) do not change much in a few days, these can be eliminated as alternative explanations of effects.

To assure any finding was not due to a pollutant other than particulate matter, investigators chose the control day to be one that also had the same

concentration of either ozone, sulfur dioxide, carbon monoxide, or nitrogen dioxide. Since the control day and the day of death had the same concentration of the other pollutant, any correlation with particles cannot be due to the other pollutant. **The study found that no matter which other pollutant was matched, PM₁₀ was associated with an increased risk of premature death.**

The author concludes that *“this adds to the considerable evidence developing from epidemiology, toxicology, and control human exposure studies indicating a causal relationship.”*

This paper also discusses two factors that might have led to the lower risk levels reported in the National Morbidity, Mortality and Air Pollution Study (NMMAPS). The first is that NMMAPS analyzed cities where PM₁₀ was monitored only every sixth day, which can lead to underestimates of effect. The second is that the NMMAPS model used a large number of “degrees of freedom” in the statistical analysis which seems to produce lower estimates.

Schwartz, J. Is the association of airborne particles with daily deaths confounded by gaseous air pollutants? An approach to control by matching. *Env Health Persp* 2004;112:557-561.

Reducing Particulate Air Pollution Could Prevent Thousands of Premature Deaths in European Cities

“Apheis” is a public health surveillance system established in 1999 in 26 European cities to provide information on air pollution and health. Using PM₁₀ data from 104 monitoring stations and 19 European cities, researchers analyzed the acute and chronic effects of particles on premature mortality.

Annual mean PM₁₀ concentrations ranged from a high of 73µg/m³ in **Bucharest** to a low of 14 µg/m³ in **Gothenburg** and **Stockholm**.

The analysis found that reducing long term exposure to PM₁₀ by 5 µg/m³ would have prevented between 3300 and 7700 early deaths annually, 500 to 1000 of which are associated with short term exposure.

According to the authors, the results show that *“even small reductions in air pollution levels could prevent a large number of deaths in the European population.”*

Medina S, Plasencia A, Mücke HG, Schwartz J, on behalf of the Apheis group. Apheis: public health impact of PM₁₀ in 19 European cities. *J Epidemiol Community Health* 2004;58:831-836.

No Threshold Evident in PM-Mortality Relationship

Numerous time-series studies have suggested a linear relationship between concentration and daily mortality over the entire range of ambient PM₁₀ concentrations in the U.S. That is, there appears to be no concentrations, or

threshold, below which adverse effects are not observed.

This study, part of the National Morbidity, Mortality, and Air Pollution Study (NMMAPS), used new statistical methods to explore the concentration-response relationship between PM₁₀ and daily mortality in the 20 largest U.S. cities. The health endpoints included daily mortality from all causes excluding accidents, cardiovascular and respiratory causes combined, and other causes. The cities studied included **Los Angeles, New York, Chicago, Dallas-Ft. Worth, Houston, San Diego, Santa Ana-Anaheim, Phoenix, Detroit, Miami, Philadelphia, Minneapolis, Seattle, San Jose, Cleveland, San Bernardino, Pittsburgh, Oakland, Atlanta, and San Antonio.**

Investigators used two different statistical models to try to identify a possible threshold concentration below which an effect of PM₁₀ on mortality could not be detected. They reported that for total mortality and mortality from cardiovascular-respiratory causes, there was no evidence of a threshold down to daily ambient concentrations of PM₁₀ as low as 10 µg/m³. They concluded that linear models without a threshold are appropriate for assessing the effect of air pollution on daily mortality.

“The present results give an indication that risk-free levels of PM₁₀ are likely lower than the present NAAQS for PM₁₀,” researchers conclude. *“In fact, the continued demonstration of adverse effects of air pollution over recent decades, even as concentrations of pollutants have declined, also suggests that exposures have not yet gone below no-effect thresholds, if such exist.”*

Daniels MJ, Dominici F, Zeger SL, Samet JM. The national morbidity, mortality and air pollution study. Part III: PM₁₀ concentration-response curves and thresholds for the 20 largest US cities. *Health Effects Institute Research Report* May 2004; Number 94, Part III.

Deaths from London Smog Episode Are Triple What is Generally Reported

“The London smog of 1952 is one of history’s most important air pollution episodes in terms of its impact on science, public perception of air pollution, and government regulation,” write the authors of a retrospective assessment of mortality from the London Smog Episode.

“The association between air pollution and health became obvious as the sharp rise in pollution was followed immediately by large increases in sickness and death.”

The elevated mortality rate continued for several months after the episode.

Initial government analyses suggested that influenza might be responsible for the high death rate in the months after the smog. This study generated estimates of the number of flu deaths using a number of methods, and concluded that only a fraction of the deaths in the months after the episode could be attributable to influenza alone.

Based on a sensitivity analysis, the authors estimate that the numbers of deaths related to air pollution following the 1952 London smog are approximately 12,000, rather than the 3,000-4,000 deaths generally reported.

The authors report that contemporary levels of air pollution in London and around the world, albeit at much lower concentrations than occurred in 1952, are still contributing to increased deaths and a substantial health burden, and cite a World Health Organization estimate of 800,000 premature deaths each year caused by urban air pollution worldwide.

Bell ML, Davis DL, Fletcher T. A Retrospective Assessment of Mortality from the London Smog Episode of 1952: The Role of Influenza and Pollution. *Env Health Persp* 2004;112:6-8.

Control of PM Substantially Diminishes Daily Deaths

Air quality in **Dublin, Ireland** deteriorated in the 1980s after a switch from oil to bituminous coal for domestic heating.

In 1990, the Irish Government banned the marketing and sale of bituminous coals within the city of Dublin. A dramatic improvement in air quality ensued. This study investigates the effect of a ban on coal sales.

Concentrations of air pollution, measured as “black smoke” and death rates were compared for 72 months before and after the ban. The analysis was adjusted to reflect age, weather, respiratory epidemics, and other factors.

Respiratory and cardiovascular death rates fell markedly following the ban on soft coal.

The authors conclude: *“Our findings suggest that control of particulate air pollution in Dublin led to an immediate reduction in cardiovascular and respiratory deaths. These data lend support to a relation between cause and the reported increase in acute mortality associated with daily particulate air pollution. Moreover, our data suggest time-series studies could be underestimating the benefits of particulate air pollution controls.”*

A follow up study presented an analysis of the medium term (weeks to months) exposure effects of particulate pollution, measured as “black smoke” and temperature, over a period of 17 years in Dublin. **Investigators found that the effects of particulate air pollution are strongest on the day of and the few days following exposure, but extend out over 40 days following exposure.** This was especially noticeable for respiratory causes of death.

“These extended follow-up effects were two to three times greater than the acute effects reported in other studies, and approach the effects reported in longer term survival studies. This analysis suggests that the studies on the

acute effects of air pollution have underestimated the total effects of temperature and particulate air pollution on mortality,” report the investigators.

Clancy L, Goodman P, Sinclair H, and Dockery DW. Effect of Air-Pollution Control on Death Rates in Dublin, Ireland: An Intervention Study. *The Lancet* 2002; 360:1210-14.

Goodman PG, Dockery DW, Clancy L. Cause Specific Mortality and the Extended Effects of Particulate Pollution and Temperature Exposure. *Env Health Persp* 2004; 112:179-185.

AIR POLLUTION AND INFLAMMATION

Breathing Air Pollution Particles Triggers Release of Inflammatory Cells From Bone Marrow

Researchers have shown that acute exposure to air pollution causes a systemic inflammation with an increase in white blood cells in the bloodstream in laboratory animals and in humans.

These white blood cells are infection-fighting cells that come from the bone marrow. The white blood cells that accumulate in the lung are predominantly monocytes (a type of white blood cell) released from the bone marrow. The function of these monocytes is to keep the lung clean by removing foreign material such as microorganisms and inhaled air pollution particles. The researchers postulate that exposure to air pollution induces the release of monocytes from the bone marrow, as part of the systemic inflammatory response to particulate air pollution.

This study was designed to explore these mechanisms in more detail. Researchers instilled two types of particles -- inert carbon, and ambient PM₁₀ into the lungs of rabbits, and measured bone marrow stimulation and the release of monocytes from the bone marrow.

The results showed that deposition of particulate matter into the lung stimulates the bone marrow to speed the release of white blood cells into the bloodstream. They also showed that the composition of the particles determines the magnitude of response.

"We suspect that these white cells such as monocytes released from the marrow by exposure to particulate matter air pollution contribute to the adverse health effects of air pollution on both the heart and lung," researchers conclude.

Goto Y, Ishii H, Hogg JC, Shih C-H, Yatera K, Vincent R, van Eeden SF. Particulate matter air pollution stimulates monocyte release from the bone marrow. *Am J Respir Crit Care Med* 2004;170:891-7.

Inflammatory Markers Decline During Antarctic Expedition

Lower levels of PM air pollution have been linked to a decrease in bone

marrow stimulation and resultant reduction in inflammatory markers in the bloodstream, in an ingenious study of Japanese explorers on an expedition to Antarctica.

A high level of atmospheric particulate matter is known to induce an increase in white blood cells and inflammatory markers in the blood. The particulate level in Antarctica is extremely low compared to that in industrial countries, so researchers devised an experiment to monitor leukocyte and cytokine levels in 39 members of the Japanese Antarctic Research Expedition during their year long stay.

Particle concentrations were measured in the city center of **Saga, Japan**, and at the Showa Research Station in **Antarctica**. Blood samples and lung function measurements were obtained the day the research vessel departed from Japan, several times during the expedition, and upon departure and after return to Japan.

Researchers found that low levels of atmospheric PM decreased circulating white blood cells and certain inflammatory markers. The results suggest that atmospheric PM provides a stronger stimulus to the bone marrow than cigarette smoking. Most measures of pulmonary function did not change, except for maximal voluntary ventilation.

Researches conclude that *“atmospheric PM level is one of the important factors affecting circulating leukocyte counts and the basal inflammatory status which are thought to be involved in the pathogenesis of cardiopulmonary disease.”*

Sakai M, Sato Y, Sato S, Ihara S, Onizuka M, Sakakibara Y, Takahashi H. Effect of relocating to areas of reduced atmospheric particulate matter levels on the human circulating leukocyte count. *J Appl Physiol* 2004; 97: 1774-1780.

Linear Dose-Response Relationship Between Ozone Exposure and Airway Inflammation

A meta-analysis of 21 human chamber studies where airway responses were assessed using bronchoscopy-based lavage (a washing of the lungs) was conducted to develop a model of ozone dose-response relationships.

Researchers observed a relatively simple linear relationship between ozone dose (which is a function of concentration, ventilation, and exposure time) and airway inflammation, as indicated by neutrophilia in bronchoalveolar lavage fluid samples, at 0-6 hours and at 18-24 hours. Linear relationships were also observed between ozone dose and protein leak into the airways over the early- and late-acute response time periods.

Researchers found that exposure to ozone concentrations at the level of the 8-hour ozone standard (0.08 ppm) at moderate ventilation rates would be sufficient to trigger an early-acute inflammatory response.

Since chamber studies use only healthy subjects, individuals with lung disease or other risk factors will experience responses at lower levels than reported in this meta-analysis, predict researchers.

Based on this preliminary analysis, researchers conclude that *“individuals performing even relatively mild exercise for prolonged periods during ozone episodes appear likely to develop acute airway inflammation.”*

Mudway IS, Kelly FJ. An investigation of inhaled ozone dose and the magnitude of airway inflammation in healthy adults. *Am J Respir Crit Care Med* 2004; 169:1089-1095.

PM_{2.5} from Smelter Region Causes Airway Inflammation in Humans

Researchers instilled relatively low masses of ambient PM_{2.5} particles through a bronchoscope into the lungs of 12 healthy volunteers.

The particle samples were collected in **Hettstedt, Germany**, a smelter town, and in **Zerbst**, a rural community 50 miles away. The sample from the smelter town was high in transition metals such as zinc, copper and cadmium.

Twenty-four hours after exposure, the lungs of participants were “washed” and the cells studied. Increased airway inflammation was observed after instillation of the Hettstedt particles.

As in an earlier series of studies in the Utah Valley, this study built on prior epidemiological and animal exposure studies of Hettstedt particles.

Researchers conclude that *“low exposure to metal-rich PM_{2.5} induces mild acute airway inflammation, which probably causes or aggravates chronic airway diseases, particularly when chronically inhaled.”*

Schaumann F, Borm PJ, Herbrich A, Knoch J, Pitz M, Schins RP, Luettig B, Hohlfeld JM, Heinrich J, Krug N. Metal-rich ambient particles (Particulate Matter 2.5) cause airway inflammation in healthy subjects. *Am J Respir Crit Care Med* 2004;170:898-903.

MISCELLANEOUS

Studies of Concentrated Ambient Particles Provide a Causal Link

The fine particle concentrator is a new technology that can capture ambient particles from the air and deliver selected concentrations to exposure chambers, where biological responses can be monitored and compared with those exposed to filtered air.

Studies of concentrated ambient particles (CAPs) have been safely performed with humans and animals, and extracts of the CAPS have been used for in vitro studies of lung cells.

Advantages of studies with concentrated ambient particles are that they use

“real-world” particles, and that they allow exposures at high enough concentrations to assess a range of responses. Disadvantages are that exposures can be variable in mass and composition from day to day and hour to hour.

Studies of human volunteers using CAPs have shown acute lung inflammation and changes in blood indices and heart rate variability.

Animal studies support potential pulmonary inflammation, blood changes, and alterations of specific cardiac endpoints. Overall, these studies have shown that ambient particles target the heart and blood vessels, in addition to the lung, and suggest that specific components in CAPs may differentially affect these tissues.

Investigators conclude that “*results have provided a causal link between PM exposure and human adverse health effects.*”

Ghio AJ, Huang Y-CT. Exposure to Concentrated Ambient Particles (CAPs): A Review. *Inhalation Toxicology* 2004;16:53-59.

Fine Particles and Gaseous Air Pollutants Increase Risk of Hospitalization

This time-series study in **Atlanta, Georgia** funded by the Electric Power Research Institute used data on more than 4 million emergency department visits from 331 hospitals, and detailed air quality data on criteria air pollutants.

For the last two years of the "ARIES" study, detailed data on several chemical characteristics of PM were available.

Researchers found evidence for an association between hospitalization for cardiovascular disease and PM_{2.5}, nitrogen dioxide, carbon monoxide, and components of PM_{2.5} including organic carbon, elemental carbon, and oxygenated hydrocarbons.

The effect of ambient pollution on cardiovascular conditions tended to be rapid, with the strongest associations observed with pollution levels on the same day as emergency department visits.

Metzger KB, Tolbert PE, Klein M., Peel JL, Flanders WD, Todd K., Mulholland JA, Ryan PB, Frumkin H. Ambient Air Pollution and Cardiovascular Emergency Department Visits in Atlanta, Georgia, 1993-2000. *Epidemiology* 2004;15:46-56.

Attaining the Ozone Standard Would Yield Billions of Dollars in Health Benefits

In 1997, EPA established a new 8-hour average standard for ozone of 0.08 ppm based on scientific studies showing that ozone caused adverse health effects at levels lower than the previous standard. EPA has published a new analysis estimating the health benefits of attaining the new standard, using the

Agency's Environmental Benefits Modeling and Analysis Program (BenMAP). The analysis uses a damage function approach similar to those used in the recent EPA regulatory impact analysis for the heavy equipment diesel rule and the proposed Clean Air Interstate Rule.

The analysis estimates that reduction of 2000-2002 ozone levels to the level of the standard would result in reductions of 800 premature deaths, 4,500 hospital and emergency room admissions, 900,000 school absences, and over a million minor restricted activity days each year. Minor restricted activity days occur when people substitute less strenuous activities or rest for their usual routines.

The study estimates the monetary value of these benefits at between \$4.9 billion and \$5.7 billion per year. The analysis notes that benefits would increase two to three times if the form of the standard did not allow any exceedances. (The current standard is based on the 4th highest 8-hour concentration averaged over 3 years.)

The authors note that the study understates likely benefits. The study assumes that ozone concentrations will only be reduced at the specific monitors currently recording exceedances, while in reality, a larger geographic region would benefit from controls. Key modeling assumptions are examined in a sensitivity analysis.

Hubbell BJ, Hallberg A, McCubbin DR, Post E. Health related benefits of attaining the eight-hour ozone standard. *Env Health Persp* 2005; 113:73-82.

Residence Near Major Roads Shortens Lifespan by 2.5 Years

This study examined the impact of air pollution relative to other causes of death.

Over 5,200 residents of **Hamilton, Ontario** in Canada were followed for a period of 10 years. A geographic information system was used to map the proximity of their homes to major urban roads and highways. Control subjects were classified as those living greater than 100 meters from a highway and greater than 50 meters from a major road. Exposed subjects were those living closer than that. For comparison purposes, data was collected on lung function, body mass index, and a diagnosis of chronic pulmonary disease, ischemic heart disease, or diabetes.

The study found that mortality rates from natural causes varied relative to proximity to traffic pollution. **Using the "rate advancement period" method, researchers found that traffic pollution shortened lives by 2.5 years.** The rate advancement period measures the impact of a risk factor on the timing of death. By comparison, chronic pulmonary disease, chronic ischemic heart disease, and diabetes were found to shorten lives by 3.4 years, 3.1 years, and 4.4 years, respectively.

Researchers concluded, *“we found an association between residential proximity to traffic and mortality. The mortality rate advancement attributable to traffic pollution was similar to that associated with chronic respiratory and pulmonary diseases and diabetes. This suggests that decreasing pollutant exposures may have a substantial public health impact.”*

Finkelstein MM, Jerrett M, Sears MR. Traffic air pollution and mortality rate advancement periods. *Am J Epidemiol* 2004;160:173-177.

Particulate Matter Causes Heritable Mutations in Mice

A team of Canadian researchers has reported that the offspring of mice exposed to particulate air pollution have an increased rate of genetic mutations, and that the mutation rate can be cut by fifty percent by cleansing the air with high efficiency particulate air (HEPA) filters.

The study builds on earlier work finding that industrial air pollution can cause elevated mutation rates in the offspring of birds and rodents.

In this study, researchers placed lab mice at an urban industrial site near two steel mills and a major highway in **Hamilton Harbour in Ontario, Canada**, as well as in a rural location 30 kilometers away, for comparison. At each location, a second set of mice was housed in a chamber equipped with a HEPA filtration system. The HEPA filtration system removes up to 99.99% of particles, down to 0.01 micrometers. Nine weeks after concluding the exposure, they bred the mice and compared the mutation rates in the offspring.

Mice exposed to HEPA-filtered air at the urban industrial site had paternal mutation rates 52 percent lower than those of the mice exposed to outside air at the same site. Through use of the HEPA filter to cleanse ambient air, researchers were able to pinpoint particulate matter as the principal factor contributing to elevated mutation rates.

While the mechanism by which particulate matter induces genetic changes is unknown, authors speculate that airborne mutagens including polycyclic aromatic hydrocarbons (PAHs) and heavy metals may be carried by particles from the respiratory system, through the bloodstream, and into the male reproductive system, harming sperm cells.

“To reduce the potential risk of harmful heritable mutations for humans and wildlife, along with a suite of other health problems, we suggest that steps be taken to reduce levels of airborne particulate matter in urban environments,” recommend the authors.

In an associated commentary, Professor of Epidemiology Jonathan Samet of Johns Hopkins University and coauthors urge caution in interpreting the findings of the study. They suggest confirmation of the findings with additional chemical substances, extending the study to examine mutations in second-

generation offspring, and additional study of mechanisms.

Somers CM, McCarry BE, Malek F, Quinn JS. Reduction of Particulate Air Pollution Lowers the Risk of Heritable Mutations in Mice. *Science* 2004;304:1008-1010.

Samet JM, DeMarini DM, and Malling HV. Do Airborne Particles Include Heritable Mutations? *Science* 2004;304:971-972.